

- sub D' 1. (Amended) [Biological material for preparing pharmaceutical compositions for treating a mammal by gene transfer, comprising, either at least a nucleic acid sequence containing a therapeutic gene and in a form enabling *in vivo* transfer of said gene into the cells of the mammal, or at least one of the mammal not naturally producing antibodies, genetically modified *in vitro* by at least a previous nucleic acid sequence, and in a form enabling its incorporation into the mammal's organism as well as optionally its previous culture; said biological material characterized by the fact that] The cell of claim 21,
- (a) wherein said nucleic acid [sequence contains] comprises a polynucleotide coding for an unmodified antibody polypeptide [gene and],
- (i) wherein the unmodified antibody polypeptide is a heavy chain or functional fragment thereof;
- (ii) wherein the antibody polypeptide does not induce an immune response sufficient for neutralizing the antibody polypeptide;
- (iii) wherein the coding polypeptide is operably linked to a promoter [elements] for expressing [in vivo said] the polynucleotide encoding the antibody polypeptide in the mammalian non-plasmocyte cell; [gene] and
- (iv) wherein the coding polypeptide is operably linked to a polynucleotide element for the secretion [in the blood circulation of a mammal of a therapeutically effective amount of this] of the antibody polypeptide from the mammalian non-plasmocyte cell [or a fragment of it, by cells of said] into a host mammal [genetically modified by said nucleic acid sequence and not naturally producing antibodies]; and
- (b) wherein the mammalian non-plasmocyte cell comprising the nucleic acid has been introduced into the host mammal.

B<sup>2</sup>

3. (Amended) [Biological material according to] The cell of claim 21, [characterized by the fact that it includes a nucleic acid sequence containing an antibody gene and elements for expressing *in vivo* said antibody gene and the secretion in the blood circulation of a mammal of a therapeutically effective amount of this antibody or a fragment of it, by cells of said mammal genetically modified by said nucleic acid sequence and not naturally producing antibodies. This] wherein the nucleic acid [sequence is a complex or] is associated with or complexed to [conjugated] with a [molecule or] carrier substance.

sub D<sup>2</sup>

4. (Amended) [Biological material according to] The cell of claim 21, [characterized by the fact that it includes a nucleic acid sequence containing an antibody gene and elements for expressing *in vivo* said antibody gene and the secretion in the blood circulation of a mammal of a therapeutically effective amount of this antibody or a fragment of it, by cells of said mammal genetically modified by said nucleic acid sequence and not naturally producing antibodies. This] wherein the nucleic acid [sequence] is a vector [permitting the effective transfer *in vivo* of the antibody gene in cells].

5. (Amended) [~~Biological material according to~~] The cell of claim 4, [~~characterized by the fact that~~] wherein the vector is a [biological] viral vector.

6. (Amended) [Biological material according to] The cell of claim 21, [characterized by the fact that it is comprised of cells not naturally producing antibodies, in a form which permits their incorporation into the mammal's organism as well as optionally its previous culture. Said cells are genetically modified by at least one nucleic acid sequence containing an antibody gene and elements for expressing *in vivo* said antibody gene and the secretion in the blood circulation of a mammal of a therapeutically effective amount of this antibody or a fragment of it] wherein the mammalian non-plasmocyte cell is genetically modified *in vitro* before being introduced into the host mammal.

B2 7. (Amended) [Biological material for the preparation of pharmaceutical compositions for the treatment of mammals with gene transfer, according to] The cell of claim 6, [characterized by the fact that] wherein the mammalian non-plasmocyte cell is [not naturally producing antibodies come] from the host mammal [to be treated].

8. (Amended) [Biological material for the preparation of pharmaceutical compositions for the treatment of mammals with gene transfer, according to] The cell of claim 6, [characterized by the fact that] wherein the mammalian non-plasmocyte cell [s not naturally producing antibodies] comes from [another] a mammal other than the host mammal [one to be treated and have undergone treatment making them compatible].

B3 11. (Amended) [Biological material according to] The cell of claim [9] 21, [characterized by the fact that] wherein the cell is [not naturally producing antibodies are] selected from the group consisting of keratinocytes, hepatocytes, [skin] fibroblasts, myoblasts, endothelial cells, and hematopoietic [stem] cells.

12. (Amended) [Biological material according to] The cell of claim 21, [characterized by the fact that] wherein the antibody [gene is a gene coding for a virgin antibody, fragment or derivative of this antibody such as] is a chimeric[al] antibody.

B4 13. (Amended) [Biological material for the preparation of pharmaceutical compositions for the treatment or prevention of cancer in a subject, in accordance with] The cell of claim 21[2], [characterized by the fact that said] wherein the antibody [, fragment or antibody derivative] is directed against a [specific] tumor cell antigen.

14. (Amended) [Biological material for the preparation of pharmaceutical compositions for the treatment or prevention of an infection or viral expansion in a subject, according to] The cell of claim 21[2], [characterized by the fact that said] wherein the antibody [fragment or antibody derivative] is directed against a [specific antigen of the] virus [responsible for said infection or against a specific antigen of cells infected by said virus].

15. (Amended) [Pharmaceutical composition comprised of a biological material according to] The cell of claim 21, [preferably associated with] in a pharmaceutically acceptable vehicle.

20. (Amended) A method of making [Manufacturing process for a cell according to claim 16, characterized by the fact that using any appropriate method, one] a mammalian non-plasmocyte cell comprising a nucleic acid containing a polynucleotide coding for an unmodified antibody polypeptide, comprising the steps of
- (1) transfer[s]ing at least one nucleic acid [sequence containing] comprising a polynucleotide coding for an unmodified antibody polypeptide [gene and],
- (i) wherein the unmodified antibody polypeptide is a heavy chain or functional fragment thereof;
- (ii) wherein the antibody polypeptide does not induce an immune response sufficient for neutralizing the antibody polypeptide;
- (iii) wherein the coding polypeptide is operably linked to a promoter [elements guaranteeing the expression *in vivo* of said] for expressing the polynucleotide encoding the antibody polypeptide in the mammalian non-plasmocyte cell; [gene] and
- (iv) wherein the coding polypeptide is operably linked to a polynucleotide element for the secretion [in the blood circulation of a mammal of a therapeutically effective quantity of this] of the antibody polypeptide from the mammalian non-plasmocyte cell [or a fragment of it, by cells of said mammal genetically modified by said nucleic acid sequence and not

B<sub>4</sub>

producing antibodies naturally in cells not naturally producing antibodies,  
and by the fact that those cells genetically modified by said nucleic acid  
sequence are chosen from among these cells];

- (2) culturing the cell *in vitro*; and  
(3) introducing the cell into a host mammal.

Kindly add new claims 21-31, as follows:

- B<sub>7</sub>
21. (New) A mammalian non-plasmocyte cell genetically modified with a nucleic acid, wherein the nucleic acid comprises a nucleotide sequence coding for an antibody molecule:
- (a) wherein the nucleotide sequence coding for the antibody molecule is operably linked to a promoter for expressing said nucleotide sequence encoding the antibody molecule in the mammalian non-plasmocyte cell, and
  - (b) wherein the nucleic acid comprises a nucleotide sequence element coding for a signal peptide operably linked to the nucleotide sequence coding for the antibody molecule, for secreting said antibody molecule from the mammalian non-plasmocyte cell into a host mammal.
22. (New) The cell of claim 21, wherein the antibody molecule is selected from a complete antibody, a single antibody heavy chain, a single antibody light chain, a chimeric antibody or a fragment thereof.
23. (New) A mammalian non-plasmocyte cell genetically modified with two distinct nucleic acids, wherein one nucleic acid comprises a nucleotide sequence coding for one fragment of an antibody molecule and the other nucleic acid comprises another nucleotide sequence coding for another fragment of an antibody molecule:

- (a) wherein each nucleotide sequence coding for the antibody molecule fragment is operably linked to a promoter for expressing said nucleotide sequence encoding the antibody molecule fragments in the mammalian non-plasmocyte cell, and
- (b) wherein each nucleic acid comprises a nucleotide sequence element coding for a signal peptide operably linked to the nucleotide sequence coding for the antibody molecule fragment, for secreting an antibody molecule made of said antibody molecule fragments from the mammalian non-plasmocyte cell into a host mammal.

24. (New) The cell of claim 23, wherein each of the two distinct antibody molecule fragments is selected from an single heavy chain antibody, a single light chain antibody or a chimeric antibody or a fragment thereof.

25. (New) A mammalian non-plasmocyte cell genetically modified with two distinct nucleic acids, wherein one nucleic acid comprises a nucleotide sequence coding for an heavy chain of an antibody molecule and the other nucleic acid comprises a nucleotide sequence coding for a light chain of an antibody molecule:

- (a) wherein each nucleotide sequence coding for a chain of an antibody molecule is operably linked to a promoter for expressing said nucleotide sequences encoding the heavy and light chains of an antibody molecule in the mammalian non-plasmocyte cell, and
- (b) wherein each nucleic acid comprises a nucleotide sequence element coding for a signal peptide operably linked to the nucleotide sequence coding for the chain of an antibody molecule, for secreting an antibody molecule made of the heavy and the light chain antibody molecules from the mammalian non-plasmocyte cell into a host mammal.

26. (New) A mammalian non-plasmocyte cell genetically modified with a nucleic acid, wherein the nucleic acid comprises one nucleotide sequence coding for one fragment of an antibody molecule and an another nucleotide sequence coding for another fragment of an antibody molecule:
- (a) wherein said first and second nucleotide sequences are separated by a nucleotide sequence permitting translation of the most downstream nucleotide sequence coding for an antibody molecule fragment for translation of both antibody molecule fragment from the same polycistronic RNA,
- (b) wherein said first and second nucleotide sequences separated by a nucleotide sequence permitting translation of the most downstream nucleotide sequence coding for an antibody molecule fragment for translation of both antibody molecule fragment from the same polycistronic RNA are operably linked to the same promoter for expressing said polynucleotides sequence encoding the antibody molecule fragments in the mammalian non-plasmocyte cell, and
- (c) wherein the nucleic acid comprises two nucleotide sequence elements each coding for a signal peptide operably linked to said first and second nucleotide sequences separated by a nucleotide sequence permitting translation of the most downstream nucleotide sequence coding for an antibody molecule fragment for translation of both antibody molecule fragment from the same polycistronic RNA, for secreting an antibody molecule made of said antibody molecule fragments from the mammalian non-plasmocyte cell into a host mammal.
27. (New) The cell of claim 26, wherein the nucleotide sequence permitting translation of the most downstream nucleotide sequence coding for an antibody molecule fragment for translation of both antibody molecule fragment from the same polycistronic RNA is an internal ribosome entry site (IRES sequence).

28. (New) The cell of claim 26, wherein each of the two distinct antibody molecule fragments are selected from an single antibody heavy chain, an single antibody light chain, or a chimeric antibody or fragment thereof.
29. (New) A mammalian non-plasmocyte cell genetically modified with a nucleic acid, wherein the nucleic acid comprises a first nucleotide sequence coding for an heavy chain of an antibody molecule and a second nucleotide sequence coding for an light chain of an antibody molecule :
- (a) wherein said first and second nucleotide sequences are separated by a nucleotide sequence permitting translation of the most downstream nucleotide sequence coding for a chain of an antibody molecule for translation of both heavy and light chains of antibody molecule from the same polycistronic RNA,
- (b) wherein said first and second nucleotide sequences separated by a nucleotide sequence permitting translation of the most downstream nucleotide sequence coding for a chain of an antibody molecule for translation of both heavy and light chains of antibody molecule from the same polycistronic RNA are operably linked to the same promoter for expressing said nucleotide sequences encoding both light and heavy chains of an antibody molecule in the mammalian non-plasmocyte cell, and
- (c) wherein the nucleic acid comprises two nucleotide sequence elements each coding for a signal peptide operably linked to each of said first and second nucleotide sequences separated by a nucleotide sequence permitting translation of the most downstream nucleotide sequence coding for an antibody chain for translation of both antibody chains from the same polycistronic RNA for secreting an antibody molecule made of said heavy and light chains from the mammalian non-plasmocyte cell into a host mammal.



30. (New) The cell of claim 29, wherein the nucleotide sequence permitting translation of the most downstream nucleotide sequence coding for an antibody molecule fragment for translation of both antibody molecule fragment from the same polycistronic RNA is an internal ribosome entry site (IRES sequence).

- Sub D4  
31. (New) A method for delivering an antibody to the blood system of a host mammal, comprising:
- implanting a cell into a mammal,
  - (a) wherein the implanted cell is a mammalian non-plasmocyte cell genetically modified with a nucleic acid, wherein the nucleic acid comprises a nucleotide sequence coding for an antibody molecule;
  - (b) wherein the nucleotide sequence coding for the antibody molecule is operably linked to a promoter for expressing said nucleotide sequence encoding the antibody molecule in the mammalian non-plasmocyte cell; and
  - (c) wherein the nucleic acid comprises a nucleotide sequence element coding for a signal peptide operably linked to the nucleotide sequence coding for the antibody molecule, for secreting said antibody molecule from the mammalian non-plasmocyte cell into a host mammal.

***In the Specification:***

Kindly amend the specification as follows:

On pg.1, between lines 6 and 7, insert

**--CLAIM OF PRIORITY**

This application is the United States national stage application of PCT International patent application PCT/FR98/00081, filed January 16, 1998. This application also claims priority to French patent application FR 97/00540, filed January 20, 1997.

**BACKGROUND OF THE INVENTION**

**1. FIELD OF THE INVENTION--**